

Research Article

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Debate about Liver Haemangioma Management

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Abstract

Background: Management of patients with liver giant hemangiomas, carries a great debate. The debate is regarding indication of surgical intervention, and also the way of management either enucleation or resection. Although non-operative management in recent studies has a low complication rate, still operative management play a rule in large symptomizing haemangioma.

Patients and Methods: A retrospective study on 49 patients with giant haemangioma between 2014 and 2018 in Advanced Hepato-Pancreatico-Biliary Center, Zagazig University Hospital, Egypt.

Results: From 49 patients, 27 patients managed conservatively. While 22 patients managed by surgery (13 by enucleation and 9 by liver resection). During the follow-up period; in the non-operative group; 5 had new onset of symptoms related to haemangioma. While in the operative group no recurrence occurred and the rate of postoperative complication was 24.49%.

Conclusion: Rigorous clinical observation is recommended in patients with giant haemangiomas. Severe symptomizing patients should manage surgically.

Keywords: Clinical observation; Enucleation; Haemangioma; Liver; Resection

Introduction

Liver Hemangioma is considered the most common benign tumor, it could be found in the general population (3% to 20%) [1]. young adult females, are the most affected patients with liver haemangioma [2]. the pathogenesis of hepatic hemangiomas is still questionable, high incidence in female patients may be attributed to hormone levels, and exposure to high levels of estrogen and progesterone, which faced in multiparity, pregnancy, and use of oral contraceptive use [3]. Haemangiomas usually discovered accidentally in routine ultrasonography used to screen liver nodules. Multiphasic CT clarifies peripheral nodular enhancement and typical centripetally progressive enhancement. Sure, diagnosis needs using magnetic resonance imaging to define the precise anatomical relationship of Glissonian pedicles and hemangiomas [4].

Mostly hemangiomas discovered accidentally as small, asymptomatic hepatic focal lesions with normal liver functions. Usually giant liver hemangiomas defined as hepatic focal

lesions more than 5 cm in diameter (Some authors suggest more than 10 cm). Often, haemangiomas managed via close clinical observation [5,6]. Conversion from conservative management to surgical intervention decided when facing progressive abdominal discomfort, rupture (spontaneous or traumatic), progressive enlargement, Kasabach-Merritt syndrome and uncertain diagnosis [7]. Liver resection, enucleation, hepatic artery ligation and liver transplantation considered the possible four types of surgical procedures [7]. But still resection and enucleation the most commonly used. Surgeons usually choose enucleation of liver hemangioma due to lower intra-operative bleeding, lower overall complications, and shorter hospital stay [8,9]. Here in our study, we evaluated the results and complications of clinical observation and surgical management of giant haemangioma of the liver.

Patients and Methods

Between June 2014 and August 2018, 49 patients diagnosed as giant haemangiomas were managed at the Advanced Hepato-Pancreatico-Biliary Center, Zagazig University. Indications of surgery were severe abdominal pain, enlarging tumor size, compression symptoms and Kasabach-Merritt syndrome. The collected data including patient's demographic data, haemangioma

characters (size, number and location), preoperative liver function, operative data (operative time, blood loss, blood and plasma transfusion, length of hospital stay) and postoperative complications and follow-up were recorded. We used MRI for all patients for diagnosis.

Surgical Technique

Prophylactic anti-coagulant was given to all patient's preoperative. Thoracic epidural catheter was applied to control postoperative pain. Surgery was performed through J shaped incision (It could be extended to bilateral subcostal with mid line extension). After mobilization of the liver, Pringle's maneuver was ready to use if needed to reduce bleeding during surgery by alternating 15 minutes of ischemia with 5 minutes of reperfusion. Enucleation or resection were performed using combination of harmonic scalpel and Kelley forceps. Enucleation was performed by dissecting the tumor from the surrounding hepatic parenchyma along the plane of the tumor capsule. Hepatic resection was carried out by removing the hepatic parenchyma containing the haemangioma, and blood vessels and bile ducts were ligated and divided as necessary. Tube drain was placed at the resection bed to detect post-operative bile leak or bleeding. The entire specimens were sent for histopathology to confirm the diagnosis.

All patients were followed up for two years by clinical examinations, liver function tests, and liver Ultrasonography at 6-month intervals during the first year and yearly thereafter. For patients with surgical intervention, laboratory investigation and radiological assessment as CT or MRI was done after 6 months to assess liver regeneration and after 2 years to assess recurrence (Figures 1-3).

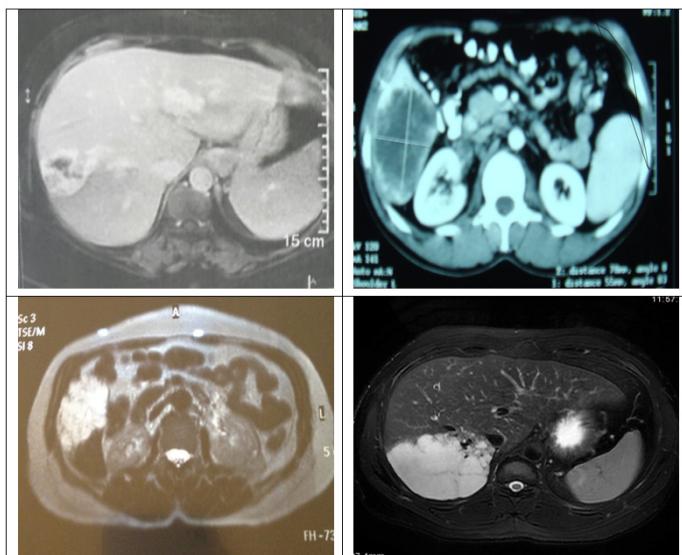


Figure 1: Haemangioma (clinical observation).

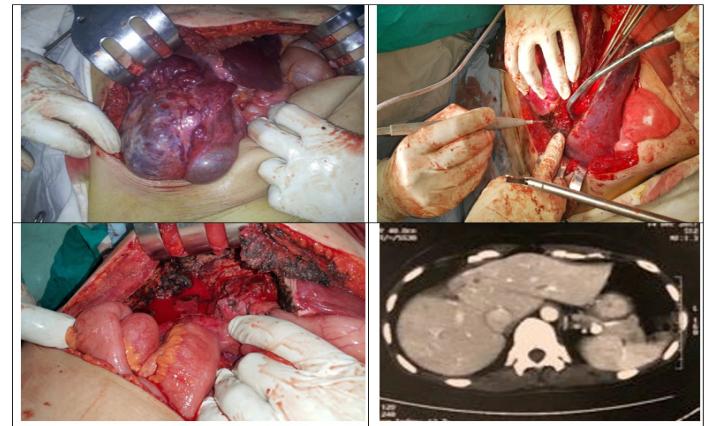


Figure 2: Female patient 45 yrs old with central haemangioma. A. Central haemangioma. B. During enucleation. C. Surgical bed. D. CT 2 yrs follow up.

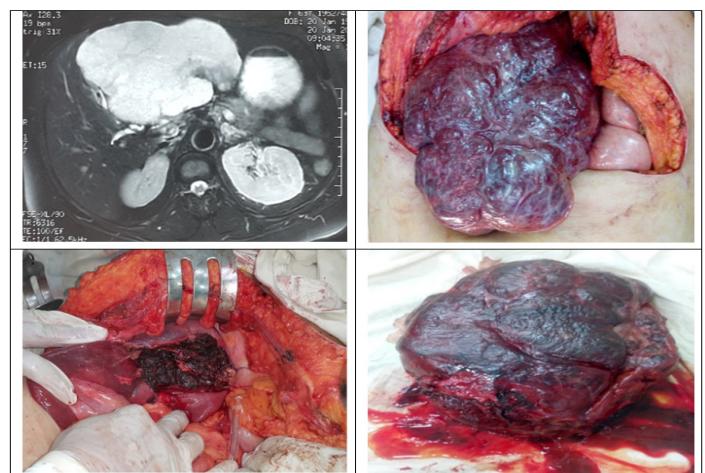


Figure 3: Female patient 50 yrs old with segment II,III haemangioma. A. MRI (peripheral haemangioma). B. Haemangioma segment II,III. C. Surgical bed. D. Haemangioma specimen.

Results

Thirty-nine (79.6%) of our patients were females while 10 (20.4%) were males. The mean age at diagnosis was 36.43 ± 11 years. Most of our patients (69.7%) were symptomatic and abdominal pain was the most common symptom presented in 21 (42.86%) patients. 40 (81.6%) patients had no past medical history.

The total number of haemangiomas for all patients was 62 lesions; 40 patients (81.6%) had single lesion. Most of our lesions were located in the right lobe (51%) with mean tumor size 11.99 ± 4.35 cm. 27 patients were managed non-operatively while 22 patients managed operatively (9 patients underwent resection and 13 patients underwent enucleation) (Tables 1,2).

P-value	Surgical (22 patients) (44.9%)		Conservative 27 patients (55.1%)	All patients 49 patients (100%)	Demographic data:
	Enucleation	Resection			
	13	9	27	49	Patients Nu: (49)
0.127	40.352±9.207	39.588±7.811	41.117±8.526	36.43±11.64	Age: (mean ±SD)
	3 10	3 6	4 23	10 39	Sex: <ul style="list-style-type: none"> Male Female
0.022*	-- 13 9 4 2 1 1	-- 9 4 5 2 2 1	15 12 8 -- 3 1 --	15 34 21 9 7 4 2	Symptoms: <ol style="list-style-type: none"> Asymptomatic: Symptomatic: <ul style="list-style-type: none"> Abdominal pain Abdominal mass Upper abdominal discomfort Biliary colic Kasbach Merritt syndrome
0.887	10 2 1 -- --	7 1 -- 1 --	23 -- -- -- 4	40 3 1 1 4	Past medical history: <ul style="list-style-type: none"> Non Hypertension DM DM + Hypertension HCV +ve
0.00* 0.018* 0.604 0.560 0.228 0.029*	10.115±1.26 199.23±70.292 26.538±7.434 21.538±6.765 1.023±0.173 1.1±0.182	10±1.391 183.333±71.589 23.888±6.233 18.222±5.607 1.055±0.101 1.1222±0.139	11.629±0.926 237.777±37.347 24.111±8.073 19.481±8.144 0.977±0.101 1.0185±0.048	10.93±1.34 217.55±58.18 24.71±7.53 19.79±7.34 1.0041±0.13 1.0592±0.12	Preoperative data: <ul style="list-style-type: none"> HB % Platelet ALT AST Total bilirubin INR

Table 1: Demographic data of all patients had haemangiomas.

Non-Operative Group (N=27)

12 patients (44.44%) had symptoms attributed to the haemangioma at diagnosis. While 15 (55.56%) were asymptomatic. single focal lesions were the predominant with a mean size 7.46±1.658 cm. Most of the lesions were peripheral and presented in the right lobe.

P-value	Surgical (22 cases)		Conservative (27)	All patients (49)	Haemangioma characters
	Enucleation (13)	Resection (9)			
0.423	14 lesions 12 1 -- --	10 lesions 8 1 -- --	38 lesions 20 4 2 1	62 lesions 40 6 2 1	Lesions Nu: <ul style="list-style-type: none"> 1 2 3 4

0.00*	18.612±3.854	14.549±4.957	7.46±1.658	11.99±4.35 cm	Size: (mean ±SD)
	2	3	38	44	• 5-10cm
	10	5	--	14	• 10-20cm
	2	2	--	4	• >20cm
0.225	4	2	4	10	Site:
	2	4	8	14	• bilateral
	7	3	15	25	• Left lobe
	9	5	21	35	Location:
	4	4	6	14	• Peripheral
					• Central

Table 2: Haemangioma characters of all patients.

Operative group: (n=22 patients)

Indications for Operation

- 7 patients with severe abdominal pain.
- 5 patients with Considerable increase in size & abdominal pain.
- 4 patients with Abdominal mass.
- 2 patients with Kasbach Merritt syndrome.
- 5 patients with abdominal pain & gastrointestinal symptoms.

In the Liver Resection Group, Were Performed

- Left lateral hepatectomy in 4 patients.
- Left formal hepatectomy in 2 patients.
- Right posterior sector resection in 2 patients.
- Right formal hepatectomy in 1 patient.

Right lobe lesions were more treated with enucleation (7 patients). The size of lesions of enucleation was high (18.61±3.8 cm) in relation to the resection group and conservative group ($p=0.00$). The HB % level, platelet count and INR were significantly different between the operative group and non-operative group ($p<0.05$). No statistically significant relationship between the types of surgical approach and blood loss, or blood product used was observed. Operative time, inflow control, ICU stay, whole hospital stays and postoperative complications were also similar for both groups (Tables 1-3). Twelve (24.49%) patients were suffered from postoperative complications. All of our complicated patients were managed conservative except one case of incisional hernia that needed mesh repair after 9 months from operation. The most common complication was pleural effusion, which occurred in 5 (10.2%) patients (Table 3).

P-value	Enucleation (13)	Resection (9 patients)	Operative (22)	Association:
		Left lateral (4) Left formal (2) Right post. (2) Right formal (1)		
	1	2	3	<ul style="list-style-type: none"> • Cholecystectomy • Splenectomy
	1	1		

0.190	160.796±45.909 min	198.888±85.651 min	176.36±66.08 min	Operative time:
0.424	738.461±489.112 ml	916.666±523.211 ml	811.36±499.03 ml	Blood loss:
0.705	2.615±1.75	2.888±1.45	2.72±1.6	PRBCs transfusion:
0.625	3.651±1.89	3.451±1.65	3.65±1.98	FFP transfusion:
0.889	7.307±2.25 days	7.444±2.18 days	7.36±2.17 days	Hospital stay:
0.450	(8) 0.846±0.8	(7) 1.11±0.78	(15) 0.954±0.785	ICU stay:
0.001*	11 2	6 3	17 5	Inflow control: • Yes • No
0.227	7 - 4 1 1 1 - 2	5 - 1 1 1 2 1 -	12 1 5 2 2 3 1 2	Complications: • Bile leak • Pleural effusion • Ascites • Paralytic ileus • Wound infection • Incisional hernia • Chest infection

Table 3: Operative data and postoperative complications.

Follow-Up (Table 4 A, B)

All the patients were followed up for two years. Data regarding the follow-up were available for all patients. Clinical observation, radiological and laboratory investigations were done at 6 m, 12 ms and 24 ms. Data revealed no abnormality in the liver function test for all patients. No mortality and no recurrence in the operative group. No change in the size of haemangioma in the non-operative group in 24, 23 and 22 patients at 6 m, 12 ms & 24 ms respectively. Favorable outcome was in 87.8%, 91.8%, and 81.6% at 6 m, 12 m & 24 ms respectively.

		N	%
2 years	• No change.	22	44.9
	• No recurrence.	22	44.9
	• Gallbladder stones.	1	2.0
	• Increased (2 need enucleation).	5	10.2
	• New 2 small haemangiomas.	1	2.0
	• New abdominal pain.	2	4.1
	• New upper abdominal discomfort.	1	2
Overall	❖ Favorable.	40	81.6
	❖ Not.	9	18.4

Year	• No change.	23	46.9
	• No recurrence.	22	44.9
	• Increased.	4	8.2
	• Abdominal pain.	1	2
Overall	❖ Favorable.	45	91.8
	❖ Not.	4	8.2
6 month	• Enlarge.	3	6.1
	• Abdominal pain.	2	4.1
	• Gall stones (lap. Cholecystectomy).	1	2
	• Incisional hernia (mesh repair).	1	
	• No change.	24	48.98
	• No recurrence.	22	44.9
	❖ Favorable.	43	87.8
Overall	❖ Not.	6	12.2
	Total	49	100.0

Table 4 (A): Follow up and outcome.

In non-operative group; 7 patients developed new symptoms; 5 patients had symptoms related to haemangioma and two patients had biliary colic due to gallbladder stones. While 6 patients had increase in the size of haemangioma; 2 of them had enucleation after two years of follow-up. 2 patients also had laparoscopic cholecystectomy.

In operative group; 1 female patient (With left lateral hepatectomy) had mesh repair for incisional hernia after 6 months, and she had small haemangioma in the right side (No change in size during follow-up). 1 female patient that underwent enucleation of a central haemangioma, had two new small haemangioma after 2 years. Also, another female patient that had two lesions (One at right lobe underwent enucleation, one at the left lobe managed conservatively); increase of the left side one by 2 cms after 2 years with appearance of abdominal pain.

Resection cases			Enucleation cases			Conservative cases			Follow up
24m	12m	6m	24m	12m	6m	24m	12m	6m	
1	1	1	1			3	1	2	New symptoms
									New lesion
						4	4	3	Increase in size
9	9	9	13	13	13				No recurrence
1 Mesh repair						22	23	24	No change
						1 Lap. Chole.		1 L a p . Chole.	New event
						2 Enucleation			
9	9	8	11	13	13	20	23	22	Favorable
--	--	1	2	--	--	7	4	5	Unfavorable

Table 4 (B): Follow up and outcome.

Discussion

Management of liver hemangiomas differs from non-operative to variety of surgical and radiological procedures. According to the fact that haemangioma usually follows a benign course, its management mostly just follow up [10,11]. In our study, 27 patients underwent conservative measures with favorable outcomes during follow up. Middle aged females (Mean age at diagnosis 50 years) more commonly affected with haemangioma. Non operative management is usually associated with safe short time and also low failure rate in long term. That may be attributed to that diagnosis is made usually at average life expectancy of 30 or more years [5].

From 9% of the 233 patients managed with observation during an 11 ± 6.4 -year follow-up in a study of Schnelldorfer, et. al. [5]. Complications were compression of surrounding structures, arterio-venous shunting, and rupture or symptoms of pain, nausea, and early satiety. We had 18.5% of the 27 patients managed with observation had new symptoms, 22% of the 27 patients had increase in the size of haemangioma (2 Patients needed enucleation). Still surgical management is the only radical treatment for hemangiomas. Indication for operative management, usually the presence of symptoms [12,13]. The most common indication for surgical excision is abdominal pain. Distension of the liver capsule (Due to size increasing or intra-tumoral hemorrhage) usually the cause of pain. Palpable masses and abdominal fullness are associated with space occupation or compression caused by the lesion [11]. In our series the indication for operation were severe abdominal pain in 7 patients, considerable increase in size and abdominal pain in 5 patients, abdominal mass in 3 patients (Huge haemangioma more than 20 cm in 4 patients).

Although pain was associated with larger lesions, still the size alone is not a formal indication for surgical procedures. Some authors [8,13,14] chose to do prophylactic excision of asymptomatic large lesions, according to the fact that hemangiomas >10 cm in size may carry a greater potential for internal bleeding, further growth or rupture. This fact matching with Zhang et al study, 18 of the 86 (20.9%) patients were asymptomatic hemangiomas >10 cm, so he chose surgical procedures for fear of a greater potential for spontaneous or traumatic rupture [8]. And this was similar to our study, four patients of 22 patients that underwent surgery; had large asymptomatic haemangioma.

Some surgeons support formal liver resection [15,16], while others support enucleation [13,17]. But when comparing the 2 options they found enucleation is better in hospital stay, operative time, morbidity and intra-operative bleeding [1]. Singh et al. emphasized that enucleation is safer and quicker, with less morbidity ($p = 0.045$) [18]. Also, Kuo et al. showed 49% less intra-operative bleeding (400 ± 129 ml vs 742 ± 116 ml; $p < 0.05$) [19].

Preserving as much as possible of healthy liver parenchyma is the target when selecting a surgical procedure [8,20]. Therefore, enucleation is still the preferred surgical procedure for giant liver hemangioma. In our study, 12 of 22 patients in operative group were treated with enucleation. We found no significant difference between liver resection and enucleation regarding operative time, vascular inflow occlusion time and frequency, blood loss, morbidity and postoperative hospital stay.

Surgical treatment for hemangiomas (>10 cm) carries high risk of copious intra-operative bleeding [14,15]. In Memorial Solan Kettering Cancer Center, 10 (19.2%) patients had blood loss of $>1L$ [21]. In our series, 7 (31.8%) patients of operative group had blood loss $>1L$. Hepatic vessels interference and site of haemangioma, strongly affect blood loss [21]. But Fu, et. al. [22] reported that centrally hemangiomas enucleation was associated with much blood loss and blood transfusions, then peripherally lesions. And this was similar to our study. At the end it must be emphasized that recurrence and rapid growth of remaining lesions are rare. In our operative group (22 patients), no recurrence had been detected in the two years follow-up. Also, the lesions that left behind didn't progress rapidly during follow up (1 enucleation, 1 resection). Most of the complications were minor and managed conservatively.

Conclusion

Clinical observation is the role in management patients with giant haemangiomas, except patients with persistent severe symptoms or development of complication. Enucleation and liver resection are safe and effective for giant haemangiomas >10 cm and complicated haemangiomas. No major differences in outcomes between enucleation and liver resection. Still clamp fracture may be used in surgical management, but hemostatic strategies including hepatic inflow occlusion decrease CVP and usage of hemostatic devices should be used to decrease the intra-operative bleeding [8].

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